What is claimed is:

1. An isolated polynucleotide encoding a mammalian Synaptic GTPase Activating Protein (SYNGAP).

2. The polynucleotide of claim 1, wherein the polynucleotide comprises the sequence of any one of SEQ ID Nos. 1-2, 4-5, or 7-8.

3. The polynucleotide of claim 1, wherein the mammalian SYNGAP has a molecular weight of between about 100 kDa to about 140 kDa as determined by polyacrylamide gel electrophoresis.

4. The polynucleotide of claim 1, wherein the polynucleotide has at least about 70 percent sequence identity to any one of SEQ ID Nos. 1-2, 4-5, or 7-8.

5. The polynucleotide of claim 1 wherein the polynucleotide is cDNA or RNA.

6. An isolated polynucleotide that is capable of hybridizing to any one of the sequences shown in SEQ ID Nos. 1-2, 4-5, or 7-8 under moderate stringency conditions.

7. The isolated polynucleotide of claim 6, wherein the polynucleotide hybridizes to to any one of the sequences shown in SEQ ID Nos. 1-2, 4-5, or 7-8 under high stringency conditions.

8. The polynucleotide of claim 7, wherein the polynucleotide is between about 12 to about 50 nucleotides in length.

9. The polynucleotide of claim 7, wherein the polynucleotide is between about 100 to about 3500 nucleotides in length.

10. The polynucleotide of claim 9, wherein the polynucleotide encodes an amino acid sequence that is capable of activating Ras GTPase by at least about 20% in a standard Ras GTPase assay.

11. The polynucleotide of claim 10, wherein the polynucleotide encodes an amino acid sequence capable of binding a PDZ domain as determined by a standard PDZ domain binding assay.

12. The polynucleotide of claim 11, wherein the polynucleotide encodes an amino acid sequence capable of binding an NR1 subunit of an NMDA receptor as determined by a standard NMDA receptor binding assay.

13. The polynucleotide of claim 12, wherein the amino acid sequence encoded by the polynucleotide comprises at least a RAS GTPase activating protein (GAP) domain and a C-terminus comprising the following amino acid sequence: (T or S) X V; wherein X is an amino acid.

14. The polynucleotide of claim 13, wherein the amino acid sequence encoded by the polynucleotide further comprises a pleckstrin homology (PH) and a C2 domain.

15. The polypeptide of claim 14, wherein the amino acid sequence encoded by the polynucleotide comprises in an N- to C- terminus orientation: the pleckstrin homology (PH), the C2 domain, the GAP domain and the C-terminal amino acid sequence.

16. The polynucleotide of claim 15, wherein the polynucleotide encodes an amino acid sequence comprising in an N- to C-terminus orientation at least about the following amino acids of SEQ ID NO: 9: 4 to 72, 87 to 190, 266 to 502, and 1132 to 1135.

17. A polynucleotide encoding a mammalian SYNGAP as shown in any one of SEQ ID Nos : 3, 6 or 9; or a fragment or a derivative thereof.

18. The polynucleotide of claim 1, wherein the SYNGAP is a human or a rat SYNGAP.

19. A fragment or a derivative of the polynucleotide of claim 1.

20. A recombinant vector comprising the polynucleotide of claim 1 or 19.

21. A host cell comprising the polynucleotide of claim 20.

22. An isolated mammalian GTPase Activating Protein at Synapses (SYNGAP) having an apparent molecular weight of between about 100 to about 150 kDa as determined by polyacrylamide gel electrophoresis.

23. An isolated polypeptide having at least about 70 percent sequence identity to any one of the amino acid sequences of SEQ ID NOs:3, 6 or 9.

24. An isolated polypeptide having the sequence shown in SEQ ID NO. 3, 6 or 9 or a fragment or a derivative thereof.

25. A method for producing a mammalian GTPase Activating Protein at Synapses (SYNGAP), the method comprising culturing a host cell of claim 21 in medium under conditions suitable for expression of the SYNGAP in the host cell or medium.

26. An antibody or antigen-binding fragment thereof capable of binding the amino acid sequence shown in SEQ ID NO: 9, the binding being blocked by at least

about 90% by contact with the amino acid sequence shown in SEQ ID NO. 21, wherein the blocking is determined by an immunoprecipitation assay or a Western immunoblot.

27. The antibody of claim 26, wherein the antibody is a capable of binding excitatory synapses as determined by microscopy.

28. The antibody of claim 27, wherein the antibody is a monoclonal antibody or an antigen-binding fragment thereof.

29. A kit comprising:

container means comprising at least one of: 1) an antibody capable of binding mammalian Synaptic GTPase Activating Protein (SYNGAP), 2) an isolated polynucleotide comprising sequence with at least about 70% sequence homology to any of the sequences shown in SEQ ID Nos. 1-2, 4-5, or 7-8 , 3) a pair of oligonucleotide primers capable of hybridizing to the sequence shown in any one of SEQ ID Nos. 1-2, 4-5, or 7-8 under high stringency conditions; and 4) a polypeptide with at least 70% sequence homology to any one of the sequences shown in SEQ ID NO: 3, 6 or 9.

30. The kit of claim 29, wherein the container means comprises a system for: 1) treating or preventing a disorder in a mammal associated with the SYNGAP, or 2) detecting excitatory synapses in a cell or group of cells *in vitro* or *in vivo*.

31. A method for modulating excitatory synapse function in a cell or group of cells, the method comprising administering to the cells a modulation effective amount of a polynucleotide of any one of claims 1 to 20 or fragment or derivative thereof.

32. A method for modulating excitatory synapse function in a cell or group of cells, the method comprising administering to the cells a modulation effective amount of the SYNGAP of any one of claims 21 to 24 or fragment or derivative thereof.

33. The method of claim 31 or 32, wherein the modulation comprises an increase excitatory synapse number as determined by microscopy or centrifugation.

34. A method for treating a disorder associated with mammalian GTPase Activating Protein at Synapses (SYNGAP) comprising administering to a patient suffering from or susceptible to such disorder an effective amount of an isolated polynucleotide of any one of claims 1 to 20 or fragment or derivative thereof.

35. A method for treating a disorder associated with mammalian GTPase Activating Protein at Synapses (SYNGAP) comprising administering to a patient suffering from or susceptible to such disorder an effective amount of an isolated SYNGAP of any one of claims 21 to 24 or fragment or derivative thereof.

36. The method of claim 35 or 36, wherein the disorder is a neurological disorder of the central (CNS) or peripheral (PNS) nervous system.

37. The method of claim 36, wherein the CNS disorder is at least one of an affective disorder, a cognitive disorder, or a neurodegenerative disorder.

38. The method of claim 37, wherein the affective disorder is depression.

39. The method of claim 37, wherein the cognitive disorder is at least one of memory loss, a learning disability, or schizophrenia.

40. The method of claim 38, wherein the learning disability is attention deficit disorder (ADD).

41. The method of claim 37, wherein the degenerative disorder is at least one of Parkinson's disease (PD), Huntington's disease (HD), senile dementia, or Alzhemier's disease (AD).

42. The method of claim 36, wherein the PNS disorder is amyotrophic lateral sclerosis.

43. The method of claim 37, wherein the neurological disorder is associated with at least one of trauma, an immune response or ischemia.

44. A method for identifying a compound useful in the diagnosis or treatment of a disorder relating to Synaptic GTPase Activating Protein (SYNGAP), the method comprising:

a) culturing cells capable of forming synapses comprising SYNGAP under conditions conducive to forming or maintaining synapses,

b) contacting the cells with a candidate compound,

c) analyzing the cells for an increase or decrease in the number of synapses; and

d) detecting the increase or decrease as indicative of the compound useful in the diagnosis or treatment of the disorder relating to SYNGAP.

45. A method for detecting a compound capable of modulating a Ras-activated second messenger pathway, the method comprising:

a) providing a Ras response system comprising a recombinant mammalian synaptic GTPase Activating Protein (SYNGAP),

b) contacting the Ras response system with a candidate compound,

c) analyzing the Ras response system for an increase or decrease in Ras activity; and

d) detecting the increase or decrease in the Ras activity as indicative of the compound capable of modulating the Ras-activated second messenger pathway.

46. The method of claim 44 or 45, wherein the Ras response system comprises Ras, adenylate cyclase and an isolated polynucleotide encoding the SYNGAP.

47. The method of any one of claims 44 to 46 wherein the Ras response system is provided in a host cell or a lysate thereof.

48. A method for detecting a compound capable of modulating a phospholipid-activated second messenger pathway, the method comprising:

a) providing an inositol triphosphate response system comprising a recombinant mammalian synaptic GTPase Activating Protein (SYNGAP),

b) contacting the inositol triphosphate response system with a candidate compound,

c) analyzing the inositol triphosphate response system for an increase or decrease in phospholipase C activity; and

d) detecting the increase or decrease in the phospholipase C activity as indicative of the compound capable of modulating the phospholipid-activated second messenger pathway.

49. The method of claim 48, wherein the phospholipase C is a phosphoinositide-specific enzyme.

50. The method of claim 48 or 49, wherein the inositol triphosphate response system further comprises phosphatidylinositol (PI), and an isolated polynucleotide encoding the SYNGAP.

51. The method of claim 50, wherein the inositol triphosphate response system further comprises at least one of diacylglycerol, protein kinase C, and inositol 1,4,5 triphosphate
($INSP_3$).

52. The method of claim 51, wherein the phospholipid-activated second messenger pathway is capable of at least one of calcium (Ca^{+2}) release or protein phosphorylation.

53. The method of any one of claims 48 to 52, wherein the inositol triphosphate response system is provided in a host cell or a lysate thereof

54. A method for detecting a compound capable of modulating phospholipid-dependent calcium (Ca^{+2}) binding to a mammalian synaptic GTPase Activating Protein (SYNGAP) C2 domain, the method comprising:

a) mixing the C2 domain with a phospholipid, calcium (Ca^{+2}) and (SYNGAP) or a fragment thereof comprising the C2 domain, the mixing being under conditions conducive to forming a complex,

b) contacting the mixture with a candidate compound,

c) analyzing the mixture for formation of the complex; and

d) detecting the complex as indicative of the compound capable of modulating the phospholipid-dependent binding between the calcium (Ca^{+2}) and the C2 domain of the SYNGAP.

55. The methods of any one of claims 44 to 54, wherein the SYNGAP has a sequence represented by SEQ ID NO:3, 6 or 9; or a fragment or derivative thereof.

56. A method for detecting a test amino acid sequence capable of binding a mammalian synaptic GTPase Activating Protein (SYNGAP), the method comprising contacting the test amino acid sequence with SYNGAP or the fragment or the derivative thereof under conditions conducive to forming a complex; and detecting the complex as indicative of the test amino acid sequence capable of binding the SYNGAP.

57. The method of claim 56, wherein the detecting step comprises at least one of immunoprecipitation, affinity chromatography, or a biosensor assay.

58. The method of claim 56, wherein the contacting step is performed in cells and the detecting step comprises monitoring expression of a detectable gene product.

59. The method of claim 58, wherein the cells are yeast cells.

60. The method of claim 56, wherein the detecting step comprises screening a polypeptide expression library or a combinatorial peptide library.

61. The method of any one of claims 56 to 60, wherein the complex is formed by binding between at least one PDZ domain in the test amino acid sequence and a C-terminal sequence in the SYNGAP or fragment or derivative thereof having the following sequence: (T or S) XV; wherein X is an amino acid.

62. An amino acid sequence detected by any of the methods of claims 56 to 61.

63. A method for detecting excitatory synapses in a cell or group of cells, the method comprising contacting cells or a group of cells with the antibody or antigen-binding fragment of any one of claims 26 to 29 under conditions sufficient to detect the excitatory synapses in the cells or group of cells.

64. The method of claim 63, wherein the antibody or antigen-binding fragment is detectably-labeled or is capable of producing a detectable label.

65. The method of claim 64, wherein the antibody or antigen-binding fragment is labeled with at least one of a radionuclide; a protein tag; a chromophore; a fluorescent, chemiluminescent or phosphorescent molecule.

66. The method of claim 64, wherein the antibody or antigen-binding fragment thereof is labeled with at least one enzyme capable of producing a chromophore, a fluorescent, chemiluminescent or phosphorescent molecule.

67. A method of detecting a compound capable of modulating the Ras GTPase activity of SYNGAP, the method comprising the steps of:

a) transfecting a cells with a reporter gene construct capable of being modulated by Ras-Raf (MAP kinase),

b) transfecting the cells with a polynucleotide encoding any one of the SYNGAP sequences shown in SEQ ID Nos. 3, 6, or 9,

c) contacting the cells with a candidate compound; and

d) detecting the reporter gene construct as being indicative of the compound capable of modulating the RasGTPase activity of SYNGAP.

68. A library comprising any one of the polynucleotides of claims 1 to 20.

69. A library comprising a fragment of the isolated polypeptide of claim 23.